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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/472,688 | 12/27/1999 | Richard A. Shimkets Ph.D | 15966-534C-CIP1 | 9084 |

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| EXAMINER |
|---|
| MORAN, MARJORIE A |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1631 | |

DATE MAILED: 11/26/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

| Offic Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/472,688 | SHIMKETS PH.D ET AL. | |
| | Examiner | Art Unit | |
| | Morjorie Moran | 1631 | |

*-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --*

**Period f r Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *18-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 December 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

***Election/Restrictions***

Applicant's election with traverse of Group I, claims 1-11 and SEQ ID NO: 509 in Paper No. 10, filed 6/27/01, is acknowledged. The traverse is on the grounds that the nucleic acid sequences of Groups II and III are directed to the same polynucleotides with the same polymorphic site as that of Group I, while Group IV recites the same polynucleotides, distinguished by specific hybridization properties. Applicant's arguments with regard to Groups I-IV are convincing, therefore Groups I-IV have been rejoined, and claims 1-18 are considered elected. Applicant further traverses on the ground(s) that Group XIV, directed to oligonucleotide arrays, is "encompassed" by the subject matter of Groups I-III, and that there would be no undue search burden to search Group XIV as well as Groups I-IV. This is not found persuasive because Group XIV is directed to an array whereas Groups I-IV are directed to individual isolated polynucleotides. As previously set forth in the restriction requirement of 3/22/01, an array comprises a mixture of nucleic acids; such a mixture has different properties than does single nucleic acid, and would be expected to behave differently in methods of use. In response to the argument that it would not be an undue burden to search all of Groups I-IV and XIV, applicant is reminded that a search for any one Group includes a search of both nonpatent literature and foreign patents as well as US patents. For the reasons set forth above, the examiner maintains that the restriction is proper and that it would be an undue burden to search for Group XIV as well as Groups I-IV.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18-44 and all sequences other than SEQ ID NO: 509 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Inventions, there

being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

An action on the merits of elected claims 1-17, as they read on SEQ ID NO: 509, follows.

***Priority***

If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. US applications 09/442,849; 09/442,129; and Provisional application 60/109,024 are disclosed on page 1 of the instant specification. The declaration also lists US application 09/443,199, filed 11/16/1999, which is not disclosed on the first page of the specification.

The instant application claims priority to a series of previously filed US applications, as set forth above. A comparison of the CRF's from the priority applications and the CRF of the instant application does not show that any of the applications from which priority is claimed contains a sequence which is identical to instant SEQ ID NO: 509. Neither the sequence listing nor the specification of any of 09/442,849; 09/442,149; or 09/443,199 discloses a SEQ ID NO: 509. As the priority applications do not appear to disclose any sequence which corresponds to instant SEQ ID NO: 509, priority for claims reciting SEQ ID NO: 509 in the instant application is granted only to the filing date of the instant application, of 12/27/1999.

***Drawings***

The drawings are objected to by the draftsperson, as set forth on Form PTO 948.

***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code set forth, for example, on page 23. See MPEP § 608.01.

***Double Patenting***

Applicant is advised that should claim 4 be found allowable, claims 5-6 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 4-6 limit the polynucleotide sequence of claim 1 to be 10-100, 10-90, or 10-75 nucleotides in length. Elected SEQ ID NO: 509 is only 51 nucleotides long, therefore each of claims 4-6 is actually directed to a polynucleotide sequence of 10-51 nucleotides, and are duplicative.

***Claim Rejections - 35 USC § 101***

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-18 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The specification teaches on pages 7-9 that sequences comprising one or more polymorphisms may be used in forensic identification, to establish paternity, to detect other polymorphisms, and in methods of treatment. The disclosed uses of forensic identification and paternity testing are generic to any nucleic acid comprising a polymorphic site and are not specific to elected SEQ ID NO: 509. The "usefulness" of a particular polymorphism in forensic or identity testing depends on whether the polymorphism is found (or not) in a plurality of

samples (e.g. from a crime scene and suspect(s); or from a child and potential father), therefore it is not clear which, if any, known polymorphism will be useful until the samples are evaluated. A polymorphism which is known to be found only in a particular subset of a population may useful in narrowing a range of suspects or potential fathers in forensic or paternity testing. The specification does not disclose that SEQ ID NO: 509 is one which has been found in samples used in forensic or paternity testing, or is known to be found in a specific subset of a population. The specification discloses, on page 3, that it is probable that a SNP can be found close to a "genetic locus of interest", but does not disclose any specific genetic locus of interest, nor that SEQ ID NO: 509, in particular, is known to be associated with a genetic locus of interest.

A method to detect other polymorphisms may be of scientific interest, but it would then require further experimentation to determine what specific, substantial, and credible utility, or "real-world" utility the detected polymorphism would have. A use in a method of treatment requires that one have knowledge of a nexus between the claimed sequence/polymorphism and a known disease or condition. The instant specification does not disclose that elected SEQ ID NO: 509, or its expression, regulation, etc. is known to be correlated with any known disease or condition.

A polynucleotide sequence may have utility based on a polypeptide encoded thereby. For example, insulin has a well-established utility, therefore polynucleotides encoding insulin also have a well-established utility. The specification discloses, in Table 1, that a peptide sequence putatively encoded by SEQ ID NO: 509 displays an unidentified degree of homology to one or more human growth factors. It is noted that the SwissProt sequence for KGF is disclosed to be 194 amino acids long whereas SEQ ID NO: 509 would encode a peptide of only 17 amino acids. In addition, SEQ ID NO: 509 does not comprise a start codon, therefore it is doubtful if SEQ ID NO: 509, alone, encodes any peptide. The specification teaches on page 12

that the present invention provides a large number of human cSNP's based on at least one gene product which has not been previously identified, and further teaches that four or more sequences could be clustered and assembled to make a consensus contig including an ORF. As SEQ ID NO: 509 does not comprise a start codon, it does not, in itself, comprise an ORF. It is possible that SEQ ID NO: 509 is a SNP "based on" a larger protein (gene product), as set forth on page 12. Table 1 discloses that SEQ ID NO: 509 is homologous to the human gene for KGF (SwissProt ID: P21781). A search of the prior art confirms that SEQ ID NO: 509 is homologous to a portion of a polynucleotide encoding KGF (see Figure 25 of WO 9611951). Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual

evidence is absent here. Neither the instant specification nor the prior art teaches that the peptide portion of KGF possibly encoded by SEQ ID NO: 509 has any activity, specifically as a growth factor. No utility has been set forth in the instant specification for the portion of the gene product represented or encoded by SEQ ID NO: 509.

For the reasons set forth above, the elected claims reciting SEQ ID NO: 509 do not have a specific, substantial, and credible utility, or a well-established utility.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Claims 1-18 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

Claims 9 and 17 limit the polynucleotide of claim 1 or claim 14 to be one "derived from" a nucleic acid encoding one of several named proteins. The instant specification does not teach that the peptide putatively encoded by elected SEQ ID NO: 509 is any of those recited in claims 9 and 17. The closest homology between the putatively encoded peptide and a peptide of the prior art is to a human growth factor, as set forth in Table 1. The specification does not teach that elected SEQ ID NO: 509 actually encodes any protein, or that the activity of a peptide putatively encoded by SEQ ID NO: 509 is known such that the identity of the peptide putatively encoded can be positively confirmed. Claims 9 and 17 do not limit a nucleic acid to one encoding a human growth factor. As the instant specification does not describe that a peptide putatively encoded by elected SEQ ID NO: 509 is one of those recited in claims 9 and 17, claims 9 and 17 are rejected for lack of written description.

***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 14, and 15 recite list of SEQ ID NO's in parentheses. Use of parentheses renders a claim indefinite as it is unclear whether the limitation(s) in the parentheses are intended to be positive limitation(s) of the claim. In claims 1, 14, and 15, it is unclear if applicant intends a nucleotide sequence comprising any polymorphic sequence (not necessarily those enclosed in parentheses), a nucleotide comprising a polymorphic sequence which may be found in any of the SEQ ID NO's enclosed in parentheses, or a nucleotide sequence consisting of the

one of the SEQ ID NO's enclosed in parentheses, wherein the nucleotide sequence comprises a polymorphism, therefore claims 1, 14, and 15 are indefinite. For purposes of further examination, claims 1, 14, and 15 are interpreted to be reciting a nucleotide sequence consisting of SEQ ID NO: 509, wherein SE ID NO: 509 comprises a polymorphism. Applicant should note that a claim reciting any other limitation; in particular, embodiments encompassed by a claim reciting open claim language, must be fully supported/described in the originally filed specification.

Claims 9 and 17 recite that a polynucleotide is "derived from" a nucleic acid encoding a polypeptide "related to" a particular list of proteins. It is unclear what amount or degree of derivation or relatedness is intended for a polynucleotide "derived from" another nucleic acid, nor for a polypeptide which is "related to" another, therefore claims 9 and 17 are indefinite.

Claims 1, 14, and 15 recite "a complementary nucleotide sequence", each in part c). It is unclear what the complementary sequence is intended to be complementary to, therefore each claim is indefinite. In addition, each claim recites that the "complementary sequence" comprises a sequence complementary to one or more polymorphic sequences, presumably related to the recited SEQ ID NO's. It is unclear if the sequence is intended to be complementary only to the polymorphic site, is intended to comprise any sequence fragment with complementarity to some part of the recited SEQ ID NO's, or is intended to be a nucleotide sequence consisting of a sequence complementary to one of the recited SEQ ID NO's, wherein the recited SEQ ID NO comprises a polymorphic site, therefore the claims are further indefinite. For purposes of further examination, the claims are interpreted to recite a nucleotide sequence complementary to SEQ ID NO: 509, wherein SEQ ID NO: 509 comprises a polymorphism.

Claims 1, 14, and 15 recite the term "complementary nucleotide sequence". The specification, on page 31, defines a complementary nucleic acid as one which selectively

hybridizes to a nucleic acid probe. A nucleotide sequence which hybridizes "selectively" to a probe may be one which is fully or partially complementary to the probe, therefore one skilled in the art would not know what degree of complementarity is intended by applicant for a "complementary nucleotide sequence", and the claims are indefinite.

***Conclusion***

Claims 1-18 are rejected; claims 19-44 and all sequences other than SEQ ID NO: 509 are withdrawn. The specification is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Marjorie A. Moran
Patent Examiner
November 19, 2001